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## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

Date of mailing (day/month/year) 07 December 1999 (07.12.99)
-----------------------------------------------------------------

To:  Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ÉTATS-UNIS D'AMÉRIQUE
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in its capacity as elected Office

International application No. PCT/US99/10186	Applicant's or agent's file reference 5774-01-MJA
International filing date (day/month/year) 10 May 1999 (10.05.99)	Priority date (day/month/year) 15 May 1998 (15.05.98)

Applicant AOMATSU, Akira
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1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

17 November 1999 (17.11.99)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  Maria Kirchner  Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>5774-01-MJA</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 99/ 10186</b>	International filing date (day/month/year) <b>10/05/1999</b>	(Earliest) Priority Date (day/month/year) <b>15/05/1998</b>
Applicant <b>WARNER-LAMBERT COMPANY et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

**GAMMA-AMINOBUTYRIC ACID DERIVATIVES CONTAINING, SOLID COMPOSITIONS AND PROCESS FOR PREPARING THE SAME**

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. —

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US 99/10186

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-9,12,13,16,17 relate to an extremely large number of possible compounds/products. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/products claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds/products, i.e.

Galenical compositions, which

a) comprise at least one of the exemplified actives ( gabapentin, baclofen, pregabalin)

and

b) comprise (at least one of the) specifically disclosed disclosed humectants  
and/or  
feature a composition aimed at solving the underlying problem of essentially  
suppressing lactamisation of the active (during storage) by proper selection  
of the adjuvants.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

International Application No

US 99/10186

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K31/195 A61K9/16 A61K47/18

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, Y	DE 39 28 183 A (GOEDECKE AG) 28 February 1991 (1991-02-28) the whole document ----	1, 2, 10-15
Y	PATENT ABSTRACTS OF JAPAN vol. 013, no. 061 (C-567), 10 February 1989 (1989-02-10) & JP 63 253022 A (NITTO ELECTRIC IND CO LTD), 20 October 1988 (1988-10-20) abstract ----	1, 2, 10-15
Y	EP 0 458 751 A (WARNER LAMBERT CO) 27 November 1991 (1991-11-27) the whole document ----	1, 2, 10-15
Y	US 4 952 560 A (KIGASAWA KAZUO ET AL) 28 August 1990 (1990-08-28) the whole document ----	1, 2, 10-15
		-/-

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## ° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

20 October 1999

27/10/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Fischer, W

## INTERNATIONAL SEARCH REPORT

International Application No

US 99/10186

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 084 478 A (TUCKER HOWARD ET AL) 28 January 1992 (1992-01-28) the whole document ----	1,2, 10-15
A	EP 0 376 891 A (CIBA GEIGY AG) 4 July 1990 (1990-07-04) ----	
A	US 4 126 684 A (ROBSON RONALD D ET AL) 21 November 1978 (1978-11-21) -----	

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

US 99/10186

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
DE 3928183	A 28-02-1991	AT 113272 T DE 59007550 D DK 414263 T EP 0414263 A ES 2063219 T HK 1003480 A IE 65291 B JP 3090053 A PT 95082 A,B		15-11-1994 01-12-1994 16-01-1995 27-02-1991 01-01-1995 30-10-1998 18-10-1995 16-04-1991 18-04-1991
JP 63253022	A 20-10-1988	NONE		
EP 0458751	A 27-11-1991	JP 4270216 A		25-09-1992
US 4952560	A 28-08-1990	JP 61186311 A JP 60214730 A CA 1249968 A EP 0159167 A		20-08-1986 28-10-1985 14-02-1989 23-10-1985
US 5084478	A 28-01-1992	AT 68786 T AU 594936 B AU 5326486 A CA 1256875 A DE 3682080 A DK 76086 A EP 0193303 A FI 860674 A,B, GR 860413 A IE 58932 B JP 1997639 C JP 7029964 B JP 61189243 A NZ 215180 A PT 82035 A,B US 5236953 A US 4845119 A		15-11-1991 22-03-1990 21-08-1986 04-07-1989 28-11-1991 19-08-1986 03-09-1986 19-08-1986 29-05-1986 01-12-1993 08-12-1995 05-04-1995 22-08-1986 29-08-1989 01-03-1986 17-08-1993 04-07-1989
EP 0376891	A 04-07-1990	AU 628455 B AU 4717789 A CA 2006771 A DK 673489 A JP 2221219 A NZ 231923 A PH 26730 A PT 92730 A US 5091184 A		17-09-1992 05-07-1990 30-06-1990 01-07-1990 04-09-1990 26-03-1992 28-09-1992 31-07-1990 25-02-1992
US 4126684	A 21-11-1978	AU 515341 B AU 2217177 A BE 851278 A CA 1069050 A DE 2705051 A FR 2340727 A GB 1567543 A IE 44562 B IL 51415 A JP 52099228 A NL 7701494 A		02-04-1981 17-08-1978 10-08-1977 31-12-1979 18-08-1977 09-09-1977 14-05-1980 13-01-1982 30-11-1979 19-08-1977 15-08-1977

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

US 99/10186

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4126684 A		PH 13312 A ZA 7700773 A	06-03-1980 28-12-1977

## INTERNATIONAL SEARCH REPORT

Original Application No

PCT/US 99/10186

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 6 A61K31/195 A61K9/16 A61K47/18

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, Y	DE 39 28 183 A (GOEDECKE AG) 28 February 1991 (1991-02-28) the whole document ---	1, 2, 10-15
Y	PATENT ABSTRACTS OF JAPAN vol. 013, no. 061 (C-567), 10 February 1989 (1989-02-10) & JP 63 253022 A (NITTO ELECTRIC IND CO LTD), 20 October 1988 (1988-10-20) abstract ---	1, 2, 10-15
Y	EP 0 458 751 A (WARNER LAMBERT CO) 27 November 1991 (1991-11-27) the whole document ---	1, 2, 10-15
Y	US 4 952 560 A (KIGASAWA KAZUO ET AL) 28 August 1990 (1990-08-28) the whole document ---	1, 2, 10-15
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search Date of mailing of the international search report

20 October 1999

27/10/1999

## Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

## Authorized officer

Fischer, W

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/10186

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 084 478 A (TUCKER HOWARD ET AL) 28 January 1992 (1992-01-28) the whole document ----	1, 2, 10-15
A	EP 0 376 891 A (CIBA GEIGY AG) 4 July 1990 (1990-07-04) ----	
A	US 4 126 684 A (ROBSON RONALD D ET AL) 21 November 1978 (1978-11-21) -----	

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US 99/ 10186

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 99/10186

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-9, 12, 13, 16, 17 relate to an extremely large number of possible compounds/products. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/products claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds/products, i.e.

Galenical compositions, which

a) comprise at least one of the exemplified actives (gabapentin, baclofen, pregabalin)

and

b) comprise (at least one of the) specifically disclosed disclosed humectants  
and/or  
feature a composition aimed at solving the underlying problem of essentially  
suppressing lactamisation of the active (during storage) by proper selection  
of the adjuvants.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

Serial Application No

PCT/US 99/10186

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
DE 3928183	A 28-02-1991	AT 113272 T DE 59007550 D DK 414263 T EP 0414263 A ES 2063219 T HK 1003480 A IE 65291 B JP 3090053 A PT 95082 A, B		15-11-1994 01-12-1994 16-01-1995 27-02-1991 01-01-1995 30-10-1998 18-10-1995 16-04-1991 18-04-1991
JP 63253022	A 20-10-1988	NONE		
EP 0458751	A 27-11-1991	JP 4270216 A		25-09-1992
US 4952560	A 28-08-1990	JP 61186311 A JP 60214730 A CA 1249968 A EP 0159167 A		20-08-1986 28-10-1985 14-02-1989 23-10-1985
US 5084478	A 28-01-1992	AT 68786 T AU 594936 B AU 5326486 A CA 1256875 A DE 3682080 A DK 76086 A EP 0193303 A FI 860674 A, B, GR 860413 A IE 58932 B JP 1997639 C JP 7029964 B JP 61189243 A NZ 215180 A PT 82035 A, B US 5236953 A US 4845119 A		15-11-1991 22-03-1990 21-08-1986 04-07-1989 28-11-1991 19-08-1986 03-09-1986 19-08-1986 29-05-1986 01-12-1993 08-12-1995 05-04-1995 22-08-1986 29-08-1989 01-03-1986 17-08-1993 04-07-1989
EP 0376891	A 04-07-1990	AU 628455 B AU 4717789 A CA 2006771 A DK 673489 A JP 2221219 A NZ 231923 A PH 26730 A PT 92730 A US 5091184 A		17-09-1992 05-07-1990 30-06-1990 01-07-1990 04-09-1990 26-03-1992 28-09-1992 31-07-1990 25-02-1992
US 4126684	A 21-11-1978	AU 515341 B AU 2217177 A BE 851278 A CA 1069050 A DE 2705051 A FR 2340727 A GB 1567543 A IE 44562 B IL 51415 A JP 52099228 A NL 7701494 A		02-04-1981 17-08-1978 10-08-1977 31-12-1979 18-08-1977 09-09-1977 14-05-1980 13-01-1982 30-11-1979 19-08-1977 15-08-1977

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No.

PCT/US 99/10186

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4126684 A		PH 13312 A ZA 7700773 A	06-03-1980 28-12-1977

## PATENT COOPERATION TREATY

PCT

REC'D 30 MAY 2000

WIPO

PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 5774-01-MJA	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/10186	International filing date (day/month/year) 10/05/1999	Priority date (day/month/year) 15/05/1998
International Patent Classification (IPC) or national classification and IPC A61K31/195		
Applicant WARNER-LAMBERT COMPANY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I     Basis of the report
- II     Priority
- III     Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV     Lack of unity of invention
- V     Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI     Certain documents cited
- VII     Certain defects in the international application
- VIII     Certain observations on the international application

Date of submission of the demand 17/11/1999	Date of completion of this report 26.05.2000
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Winger, R Telephone No. +49 89 2399 8129



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/10186

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-63                   as originally filed

**Claims, No.:**

1-17                   as originally filed

2. The amendments have resulted in the cancellation of:

the description,        pages:  
 the claims,              Nos.:  
 the drawings,            sheets:

3.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application.  
 claims Nos. 1-9,12,13,16,17 (in part).

because:

- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/10186

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
  
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
  
- no international search report has been established for the said claims Nos. 1-9,12,13,16,17 (in part).

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims 3-5
	No:	Claims 1,2,6-17
Inventive step (IS)	Yes:	Claims 3-5
	No:	Claims 1,2,6-17
Industrial applicability (IA)	Yes:	Claims 1-17
	No:	Claims

**2. Citations and explanations**

**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/10186

**Re Section III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The International Search Report for claims 1-9, 12, 13, 16, and 17 was only established for galenical compositions comprising at least one of gabapentine, baclofen or pregabalin in combination with at least one of the specifically disclosed humectants or a composition aimed at solving the underlying problem of essentially suppressing lactamisation of the active by proper selection of the adjuvants (cf. International Search Report, sheet PCT/ISA/210). Accordingly, the examination was carried out taking these restrictions into account.

**Re Section V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

The following statement with regard to novelty is restricted to the claims as considered by the International Search Report (see above).

2. **Prior Art:** Reference is made to the following documents cited in the International Search Report

D1: DE 39 28 183 A  
D3: EP-A-0 458 751  
D6: EP-A-0 376 891  
D7: US-A-4 126 684

3. **Novelty:** The subject-matter of claims 1, 2, and 6-17 does not seem to be novel.

Document D1 discloses cyclic amino acid derivatives including gabapentin (p 2, l 57) which are combined with suitable adjuvants, which do not catalyse lactamization. One of these adjuvants, although it reduces the stability of the cyclic amino acids, namely docosanoyl glyceride (p 4, l 11) falls within the substances claimed and hence anticipates the subject-matter of claims 1, 2, 6, 10, 12, 13, and 14.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/10186

Document D3 discloses a delivery system for cyclic amino acids (e.g. gabapentin). As excipient sorbitol (p 5, l 24), for the first coating plasticizers including glyceryl esters (p 6, l 16; examples) and for the second coating wax components including glycerides and polyglycerol esters (p 4, l 16) are used. As these components are all "combined" and the final tablets "comprise" said substances, the subject-matter of claims 1, 2, and 6-15 is anticipated. In addition document D6 discloses a pharmaceutical composition in the form of a tablet, which contains baclofen and glycerids (p 5, l 51-55).

Document D7 discloses tablets containing baclofen and diluents, e.g. sorbitol and/or glycine (p 3, l 58) hence additionally anticipating the subject matter of claims 16 and 17.

**4. Inventive step: The subject-matter of claims 3-5 seems to be inventive.**

The current application is related to stabilized solid compositions comprising a 4-amino-3-substituted-butanoic acid derivative and a humectant. It has been shown, that under certain conditions such compositions are more stable than formulations with or without other adjuvants. Document D1, which is considered to represent the most relevant state of the art, discloses also such stabilized compositions containing cyclic amino-acids and certain suitable adjuvants (cf. p 4, l 13). The subject-matter of the claims 3-5 differs from said document in that the suitable adjuvants are specific humectants. In view of D1, the problem to be solved by the present invention may therefore be regarded as finding other suitable adjuvants for the stabilization of said amino acids. Although the humectants claimed in the current application are well known in the field, there is no indication in the prior art, that they are suitable stabilizing adjuvants. Hence, the subject-matter of claims 3-5 seems to involve an inventive step.

**5. Industrial Applicability:**

The subject-matter of the claims relates to stabilized solid compositions comprising a 4-amino-3-substituted-butanoic acid derivative and a humectant which are industrially applicable under Article 33(4) PCT.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/10186

**Re Section VII**

**Certain defects in the international application**

6. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in document D1 is not mentioned in the description, nor are these documents identified therein.

**Re Section VIII**

**Certain observations on the international application**

7. In the description and in the claims the term "4-amino-3-substituted-butanoic derivative" is used both for the 4-amino-3-substituted-butanoic derivative alone (the substance according to the mentioned formula) as well as for the combination of this substance with the stabilizing humectant. Hence, the required clarity (Article 6 PCT) is missing.
8. Claim 1 is unclear, because the humectant found on page 76 has to be combined with the 4-amino-3-substituted-butanoic derivative and should not be a substituent thereof.
9. It seems to be clear from the description on page 48 that - in order to obtain a stabilizing effect - a certain molar relation (effective amount) of the humectant with respect to the butanoic acid derivative is essential to the definition of the invention. Since independent claims 1 and 12 do not contain this feature they do not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.
10. In claims 2 and 13 it is unclear, to which humectants the aliphatic esters refer to.
11. The vague and imprecise statement "scope of the invention" on p 51, I 8 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.

NOTED

NOV - 2 1999

PATENT COOPERATION TREATY

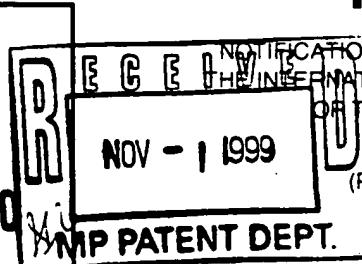
R. ARMSTRONG

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:  
WARNER-LAMBERT COMPANY  
Attn. RYAN, M. Andrea  
201 Tabor Road  
Morris Plains, New Jersey 07950  
UNITED STATES OF AMERICA

PTO/PCT Rec'd 06 NOV 2000



NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

INT'L PCT  
PATENT DEPT.

Date of mailing  
(day/month/year)

27/10/1999

Applicant's or agent's file reference

5774-01-MJA

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US 99/ 10186

International filing date

10/05/1999

Applicant

WARNER-LAMBERT COMPANY et al.

1.  The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Further action(s): The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the



European Patent Off  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2  
Fax: (+31-70) 340-3

Express Mail No. EJ881445843US  
PD-5774-01-MJA

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

**When?** Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been filed, see below.

**How?** Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

Letter (Section 205(b));

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Office, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>5774-01-MJA</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 99/ 10186</b>	International filing date (day/month/year) <b>10/05/1999</b>	(Earliest) Priority Date (day/month/year) <b>15/05/1998</b>
Applicant <b>WARNER-LAMBERT COMPANY et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:
- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

**GAMMA-AMINOBUTYRIC ACID DERIVATIVES CONTAINING, SOLID COMPOSITIONS AND PROCESS FOR PREPARING THE SAME**

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.       

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 10186

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  

see FURTHER INFORMATION sheet PCT/ISA/210
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-9,12,13,16,17 relate to an extremely large number of possible compounds/products. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/products claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds/products, i.e.

Galenical compositions, which

a) comprise at least one of the exemplified actives (gabapentin, baclofen, pregabalin)

and

b) comprise (at least one of the) specifically disclosed disclosed humectants  
and/or  
feature a composition aimed at solving the underlying problem of essentially  
suppressing lactamisation of the active (during storage) by proper selection  
of the adjuvants.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/10186

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61K31/195 A61K9/16 A61K47/18

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, Y	DE 39 28 183 A (GOEDECKE AG) 28 February 1991 (1991-02-28) the whole document ---	1,2, 10-15
Y	PATENT ABSTRACTS OF JAPAN vol. 013, no. 061 (C-567), 10 February 1989 (1989-02-10) & JP 63 253022 A (NITTO ELECTRIC IND CO LTD), 20 October 1988 (1988-10-20) abstract ---	1,2, 10-15
Y	EP 0 458 751 A (WARNER LAMBERT CO) 27 November 1991 (1991-11-27) the whole document ---	1,2, 10-15
Y	US 4 952 560 A (KIGASAWA KAZUO ET AL) 28 August 1990 (1990-08-28) the whole document ---	1,2, 10-15
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

20 October 1999

Date of mailing of the international search report

27/10/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040. Tx. 31 651 epo nl.  
Fax: (+31-70) 340-3016

Authorized officer

Fischer, W

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/10186

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
Y	US 5 084 478 A (TUCKER HOWARD ET AL) 28 January 1992 (1992-01-28) the whole document ---	1,2, 10-15
A	EP 0 376 891 A (CIBA GEIGY AG) 4 July 1990 (1990-07-04) ---	
A	US 4 126 684 A (ROBSON RONALD D ET AL) 21 November 1978 (1978-11-21) -----	

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 99/10186

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
DE 3928183	A 28-02-1991	AT 113272 T DE 59007550 D DK 414263 T EP 0414263 A ES 2063219 T HK 1003480 A IE 65291 B JP 3090053 A PT 95082 A,B		15-11-1994 01-12-1994 16-01-1995 27-02-1991 01-01-1995 30-10-1998 18-10-1995 16-04-1991 18-04-1991
JP 63253022	A 20-10-1988	NONE		
EP 0458751	A 27-11-1991	JP 4270216 A		25-09-1992
US 4952560	A 28-08-1990	JP 61186311 A JP 60214730 A CA 1249968 A EP 0159167 A		20-08-1986 28-10-1985 14-02-1989 23-10-1985
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EP 0376891	A 04-07-1990	AU 628455 B AU 4717789 A CA 2006771 A DK 673489 A JP 2221219 A NZ 231923 A PH 26730 A PT 92730 A US 5091184 A		17-09-1992 05-07-1990 30-06-1990 01-07-1990 04-09-1990 26-03-1992 28-09-1992 31-07-1990 25-02-1992
US 4126684	A 21-11-1978	AU 515341 B AU 2217177 A BE 851278 A CA 1069050 A DE 2705051 A FR 2340727 A GB 1567543 A IE - 44562 B IL 51415 A JP 52099228 A NL 7701494 A		02-04-1981 17-08-1978 10-08-1977 31-12-1979 18-08-1977 09-09-1977 14-05-1980 13-01-1982 30-11-1979 19-08-1977 15-08-1977

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US 99/10186

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4126684 A		PH 13312 A ZA 7700773 A	06-03-1980 28-12-1977

## PATENT COOPERATION TREATY

5774 PCT

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PTO/PCT Rec'd 06 NOV 2000

Rose Armstrong

PCT

To:

MANSMANN, Ivo  
 Warner-Lambert Company  
 Legal Division  
 Patent Department  
 Gödecke AG  
 Mooswaldallee 1  
 D-79090 Freiburg  
 ALLEMAGNE

Patentwesen

Eing.: 29. Mai 2000

NOTIFICATION OF TRANSMITTAL OF  
 THE INTERNATIONAL PRELIMINARY  
 EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing  
(day/month/year)

26.05.2000

Applicant's or agent's file reference  
5774-01-MJA

## IMPORTANT NOTIFICATION

International application No.  
PCT/US99/10186International filing date (day/month/year)  
10/05/1999Priority date (day/month/year)  
15/05/1998

Applicant

WARNER-LAMBERT COMPANY et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

**4. REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

h

Name and mailing address of the IPEA/

European Patent Office  
 D-80298 Munich  
 Tel. +49 89 239:  
 Fax: +49 89 239

Authorized officer

Senkel, H



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT  
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>5774-01-MJA</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US99/10186</b>	International filing date (day/month/year) <b>10/05/1999</b>	Priority date (day/month/year) <b>15/05/1998</b>
International Patent Classification (IPC) or national classification and IPC <b>A61K31/195</b>		
<p><b>Applicant</b> <b>WARNER-LAMBERT COMPANY et al.</b></p>		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input checked="" type="checkbox"/> Certain defects in the international application</li> <li>VIII <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul>		

Date of submission of the demand <b>17/11/1999</b>	Date of completion of this report <b>26.05.2000</b>
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer <b>Winger, R</b> Telephone No. +49 89 2399 8129



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/10186

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-63                   as originally filed

**Claims, No.:**

1-17                   as originally filed

2. The amendments have resulted in the cancellation of:

- the description,        pages:  
 the claims,              Nos.:  
 the drawings,            sheets:

3.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application.  
 claims Nos. 1-9,12,13,16,17 (in part).

because:

- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US99/10186

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
  
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
  
- no international search report has been established for the said claims Nos. 1-9,12,13,16,17 (in part).

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims 3-5
	No:	Claims 1,2,6-17
Inventive step (IS)	Yes:	Claims 3-5
	No:	Claims 1,2,6-17
Industrial applicability (IA)	Yes:	Claims 1-17
	No:	Claims

**2. Citations and explanations**

**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/10186

**Re Section III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The International Search Report for claims 1-9, 12, 13, 16, and 17 was only established for galenical compositions comprising at least one of gabapentine, baclofen or pregabalin in combination with at least one of the specifically disclosed humectants or a composition aimed at solving the underlying problem of essentially suppressing lactamisation of the active by proper selection of the adjuvants (cf. International Search Report, sheet PCT/ISA/210). Accordingly, the examination was carried out taking these restrictions into account.

**Re Section V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

The following statement with regard to novelty is restricted to the claims as considered by the International Search Report (see above).

2. **Prior Art:** Reference is made to the following documents cited in the International Search Report

D1: DE 39 28 183 A  
D3: EP-A-0 458 751  
D6: EP-A-0 376 891  
D7: US-A-4 126 684

3. **Novelty:** The subject-matter of claims 1, 2, and 6-17 does not seem to be novel.

Document D1 discloses cyclic amino acid derivatives including gabapentin (p 2, l 57) which are combined with suitable adjuvants, which do not catalyse lactamization. One of these adjuvants, although it reduces the stability of the cyclic amino acids, namely docosanoyl glyceride (p 4, l 11) falls within the substances claimed and hence anticipates the subject-matter of claims 1, 2, 6, 10, 12, 13, and 14.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/10186

Document D3 discloses a delivery system for cyclic amino acids (e.g. gabapentin). As excipient sorbitol (p 5, l 24), for the first coating plasticizers including glyceryl esters (p 6, l 16; examples) and for the second coating wax components including glycerides and polyglycerol esters (p 4, l 16) are used. As these components are all "combined" and the final tablets "comprise" said substances, the subject-matter of claims 1, 2, and 6-15 is anticipated. In addition document D6 discloses a pharmaceutical composition in the form of a tablet, which contains baclofen and glycerids (p 5, l 51-55).

Document D7 discloses tablets containing baclofen and diluents, e.g. sorbitol and/or glycine (p 3, l 58) hence additionally anticipating the subject matter of claims 16 and 17.

**4. Inventive step: The subject-matter of claims 3-5 seems to be inventive.**

The current application is related to stabilized solid compositions comprising a 4-amino-3-substituted-butanoic acid derivative and a humectant. It has been shown, that under certain conditions such compositions are more stable than formulations with or without other adjuvants. Document D1, which is considered to represent the most relevant state of the art, discloses also such stabilized compositions containing cyclic amino-acids and certain suitable adjuvants (cf. p 4, l 13). The subject-matter of the claims 3-5 differs from said document in that the suitable adjuvants are specific humectants. In view of D1, the problem to be solved by the present invention may therefore be regarded as finding other suitable adjuvants for the stabilization of said amino acids. Although the humectants claimed in the current application are well known in the field, there is no indication in the prior art, that they are suitable stabilizing adjuvants. Hence, the subject-matter of claims 3-5 seems to involve an inventive step.

**5. Industrial Applicability:**

The subject-matter of the claims relates to stabilized solid compositions comprising a 4-amino-3-substituted-butanoic acid derivative and a humectant which are industrially applicable under Article 33(4) PCT.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US99/10186

**Re Section VII**

**Certain defects in the international application**

6. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in document D1 is not mentioned in the description, nor are these documents identified therein.

**Re Section VIII**

**Certain observations on the international application**

7. In the description and in the claims the term "4-amino-3-substituted-butanoic derivative" is used both for the 4-amino-3-substituted-butanoic derivative alone (the substance according to the mentioned formula) as well as for the combination of this substance with the stabilizing humectant. Hence, the required clarity (Article 6 PCT) is missing.
8. Claim 1 is unclear, because the humectant found on page 76 has to be combined with the 4-amino-3-substituted-butanoic derivative and should not be a substituent thereof.
9. It seems to be clear from the description on page 48 that - in order to obtain a stabilizing effect - a certain molar relation (effective amount) of the humectant with respect to the butanoic acid derivative is essential to the definition of the invention. Since independent claims 1 and 12 do not contain this feature they do not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.
10. In claims 2 and 13 it is unclear, to which humectants the aliphatic esters refer to.
11. The vague and imprecise statement "scope of the invention" on p 51, l 8 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>A61K 31/195, 9/16, 47/18</b>		A1	(11) International Publication Number: <b>WO 99/59572</b> (43) International Publication Date: 25 November 1999 (25.11.99)
(21) International Application Number: PCT/US99/10186		(81) Designated States: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 10 May 1999 (10.05.99)			
(30) Priority Data: 10/133122 15 May 1998 (15.05.98) JP			
(71) Applicant (for all designated States except US): WARNER-LAMBERT COMPANY [US/US]; 201 Tabor Road, Morris Plains, NJ 07950 (US).			
(72) Inventor; and		Published	
(75) Inventor/Applicant (for US only): AOMATSU, Akira [JP/JP]; 34-8-302, Matsuka, Hachioji-shi, Tokyo 192-0362 (JP).		With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	
(74) Agents: RYAN, Andrea, M.; Warner-Lambert Company, 201 Tabor Road, Morris Plains, NJ 07950 (US) et al.			
(54) Title: GAMMA-AMINOBUTYRIC ACID DERIVATIVES CONTAINING, SOLID COMPOSITIONS AND PROCESS FOR PREPARING THE SAME			
(57) Abstract			
The present invention provides a stabilized solid composition containing a 4-amino-3 <sup>4</sup> -substituted-butanoic acid derivative which can be obtained by incorporating a humectant as a stabilizer.			

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W 09/674819

1664

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

1614

CORRECTED VERSION

TECH CENTER 1600  
JUN 23 2001

RECEIVED

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
25 November 1999 (25.11.1999)

PCT

(10) International Publication Number  
**WO 99/59572 A1**

(51) International Patent Classification<sup>6</sup>: **A61K 31/195**, 9/16, 47/18

(81) Designated States (*national*): AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA.

(21) International Application Number: PCT/US99/10186

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(22) International Filing Date: 10 May 1999 (10.05.1999)

Published:  
— With international search report.

(25) Filing Language: English

(48) Date of publication of this corrected version:  
21 December 2000

(26) Publication Language: English

(15) Information about Correction:  
see PCT Gazette No. 51/2000 of 21 December 2000, Section II

(30) Priority Data:

10/133112 15 May 1998 (15.05.1998) JP

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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WO 99/59572 A1

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(57) Abstract: The present invention provides a stabilized solid composition containing a 4-amino-3-substituted-butanoic acid derivative which can be obtained by incorporating a humectant as a stabilizer.